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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,893	03/13/2001	Susan Ann Bevers	11543.120	3883

7590 10/20/2004

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EXAMINER

EPPERSON, JON D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/804,893

Applicant(s)

BEVERS ET AL.

Examiner

Jon D Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 1-16, 18, 20, 23 and 25-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17, 19, 21, 22 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

1. The Response filed February 17, 2004 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 1-33 were pending. Applicants amended claims 17 and 19. No claims were added or canceled. Therefore, claims 1-33 are currently pending.
4. Claims 1-16, 18, 20, 23 and 25-33 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.
5. Therefore, claims 17, 19, 21-22 and 24 are examined on the merits in this action.
6. Please note that this application contains claims 1-16, 18, 20 and 25-33 drawn to a nonelected invention(s). This was addressed in the previous action (e.g., see Paper No. 13). A complete reply to the final rejection **must include cancellation of nonelected claims** or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Withdrawn Objections/Rejections

7. All outstanding objection and/or rejections are withdrawn in view of Applicants' arguments and/or amendments.

Maintained Rejections

8. Claims 17, 19, 21-22 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Kool et al (US Patent No. 6,479,650) (Filing Date is **December 14, 1999**).

For *claims 17, 19, 21-22 and 24*, Kool et al. (see entire document) disclose a method for visually detecting nucleic acids using fluorescent cyclic compounds joined to a carbon of a sugar molecule, which anticipates applicants elected formula i.e., B-(-L-(D)_m)_n wherein m and n are 1, B is a nucleic acid and L is a sugar analogue and D is any of the polycyclic compounds listed in the specification of '650 including a perylene imide-derivative (see Kool et al, Summary of Invention; see also column 3, paragraphs 4-7 and paragraph bridging columns 3-4; see also compounds listed in columns 6-14; see especially compound in column 9, lines 15-30; see also column 6, lines 19-25; see also abstract indicating the use of phosphoramidites i.e., an X group that would enable the attachment to a hydroxy i.e., the DNA forming a "phosphate" bond to a nucleic acid), which anticipates claims 17, 19, 21-22 and 24. Kool et al. does not state that perylene imides derivatives listed on column 9 have absorption and/or emission in the visible range or a molar extinction coefficient of at least about 40,000 M⁻¹cm⁻¹, but the perylene imides do possess the same structure as that currently claimed by Applicants in their most preferred embodiments (e.g., see claim 24) and, as a result, the compounds would be

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expected to possess the same physical properties (i.e., the properties would be inherent because both disclose/claim the same perylene bisimide structures). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

Response

9. Applicant’s arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants’ newly amended and/or added claims and/or arguments.

Applicants argue, “Applicants’ Claims 17 and 19, as amended, differ from the method disclosed by Kool because the visually detectable biomolecules of Applicants’ method have a molar extinction coefficient of at least $40,000 \text{ M}^{-1}\text{cm}^{-1}$, whereas the fluorescently labeled biomolecules disclosed by Kool generally have molar extinction coefficients of less than $35,000 \text{ M}^{-1}\text{cm}^{-1}$. The one exception is biomolecule 3c. However, biomolecule 3c has an absorption maximum of 285 and an emission maximum of 345 nm. Therefore, biomolecule 3c of Kool does

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not absorb and emit light in the region of the spectrum ranging from about 400 nm to about 800 n, and thus, is not visually detectable as defined in Applicants' specification (e.g., see 2/17/04 Response, pages 24-25, especially page 24, second to last paragraph).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants do not consider the bis-amide derivatives (e.g., see Kool et al., column 9) and, as a result, Applicants' arguments are moot. The compounds to which Applicants refer (i.e., see Table I) disclose spectral data ONLY for compounds 3a-e, pyrene butyric acid and terthiophene (e.g., see Table I; see also figure 1 showing structures of compounds 3a-3d). Thus, the spectral data for the bis-amides is not provided. Consequently, the Examiner contends that it is Applicants burden to prove that these bis-amides do not possess the requisite spectral properties as outlined in the amended rejection above.

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 102

10. Claims 17, 19 and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Fourrey et al. (Fourrey, J.L.; Varenne, J.; Blonski, C.; Dousset, P.; Shire, D. "1,1-Bis-(4-Methoxyphenyl)-1'-pyrenyl methyl (bmpm): A new fluorescent 5' protecting group from the purification of unmodified and modified oligonucleotides" *Tetrahedron Letters*, 1987, Vol. 28, No. 43, pp 5157-5160).

For *claims 17, 19 and 21-22*, Fourrey et al. (see entire document) disclose **(a)** pyrenyl conjugates that fall within the scope of $B-(L-(D)_m)_n$ (e.g., see figure 1A and reference 14 wherein a 5'-bmpm-30 based oligodeoxynucleotide is disclosed, 5'-bmpm-TCCCTCTTGAAGGAAACCAGCCAGTGCCAC; B = 29-mer; L = linear portion of the 5' T, D = pyrenyl modified dimethoxytrityl, m and n = 1, X = phosphoramidite which enables attachment to the 5'-OH of the adjacent C in the 30 mer shown above to produce a "phosphate" bond) and also disclose **(b)** detecting said pyrenyl conjugate by its "visible" properties (e.g., see figure 2; see also page 5160, reference 8 showing emission maximum at 396 nm, which is "about" 400 nm). The reference does not state whether or not said bmpm group has a molar extinction coefficient of at least about $40,000 \text{ M}^{-1}\text{cm}^{-1}$, but does state, "they could detect quantities of bmpmT down to 10^{-10} M on silica gel tlc plates," which indicates very strong fluorescence intensity. In addition, the bmpm group contains a "pyrene derivative", which represents one of Applicants' preferred embodiments (e.g., see withdrawn claim 20). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

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11. Claims 17, 19 and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Randolph et al. (Randolph J.B.; Waggoner, A.S. "Stability, specificity and fluorescence brightness of multiply-labeled fluorescent DNA probes" Nucleic Acids Research 1997, 25, 14, 2923-2929) as evidenced by SyntheGen (SyntheGen Online Catalog, 2004, Cy3 product specifications, pages 1-2). Please note that MPEP § 2131.01(c) permits the use of multiple reference in a 102 rejection to show inherency.

For *claims 17, 19 and 21-22*, Randolph et al. (see entire document) disclose **(a)** singly labeled Cy3 uridine conjugates, C2dT or C6dT (e.g., see figure 1B), or multiple substituted Cy3 polyT conjugates (e.g., see figure 1C) that fall within the scope of B-(L-(D)_m)_n (e.g., see figures 1 B-C wherein B = modified uridine or a nucleic acid probe shown in figure 1C; L = -(CH₂)₅-C(=O)- (e.g., see figure 1A/B wherein D = is a uridine monomer or one of the nucleic acid probes listed in figure 1C, m and n = 1 for cy3 labeled uridine analogues, c2dT or C6dT, or m = 1 and n varies depending on the oligomer shown in figure 1C, X = N-hydroxysuccinimidyl ester which enables attachment to an amine to form an amide; see also page 2924, column 2, paragraph 2, "The fluorophores were attached through the formation of an amide bond between the primary amine of linker and the active N-Hydroxysuccinimidyl ester"; see also page 2925 wherein the Cy3-labeled probes are shown to have an emission λ_{max} at 552 nm, which is in the visible range, and a molar extinction coefficient $> 40,000 \text{ M}^{-1} \text{ cm}^{-1}$). In addition, Randolph et al. also disclose **(b)** detecting said Cy3 conjugate by its "visible" properties (e.g., see figure 2; see also Table 1).

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In the alternative that Table 1 of Randolph et al. does not adequately address the spectral requirements of the current claim, the Examiner further submits the Synthegeen online catalog to prove that Cy3 would inherently possess the claimed spectral requirements. For example, Synthegeen disclose Cy3 Excitation Max(nm) and Emission Max(nm) at 552 and 570 nm, respectively, which clearly fall within the "visible" spectrum. In addition, the Extinction coefficient Max is 150,000 and the Extinction Coefficient at 260 nm is 40,500 both of which meet the at least about 40,000 $M^{-1}cm^{-1}$ (e.g., see Synthegeen online catalog, 2004, page 2).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
October 3, 2004

BENNETT CELSA
PRIMARY EXAMINER

